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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/838,785	04/20/2001	Ted Lau	51831AUSM1	9790

7590 12/17/2003

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/17/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/838,785	LAU ET AL	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *1-27, 30-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 28-29 are being examined.

This application contains claims drawn to an invention nonelected with traverse in Paper No.7. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The following are the remaining rejections.

OBJECTION

Claim 28 is objected to because claim 28 is now amended to recite a method for selectively destroying a "prostate-derived" cell expressing SEQ ID NO:2. It is not clear how the cell is derived from the prostate.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Rejection under 35 USC 112, first paragraph of claims 28-29 pertaining to lack of enablement for a method for selectively destroying a prostate-derived cell, or a method for treating prostate cancer remains for reasons already of record in paper No.10.

Applicant argues that at the time the invention was made, there were many examples of immunoconjugates comprising antibodies and toxins being used to selectively kill cells, e.g. US 5,863,745, US 6,099,842, Liu et al, 1996, Bera et al, 2001.

Applicant argues that concerning the reference cited by the Examiner, WO 93/17715, it is not surprising that in a patent application, the inventors would point out the problem which could arises with other methodologies. Applicant asserts that the claimed invention uses the same principles as those of WO 93/17715, only with the use of a different target. Applicant further argues that the article by Gutheil et al, 2001, teaches approaches which can be taken to address the issues cited by White et al, and that those skilled in the art at the time the invention was made were aware of these issues. Applicant argues that it would be normal during the process of drug development to refine the use of the therapeutic candidate, and one skilled in the art had the knowledge to realize the therapeutic usefulness of the claimed invention.

Applicant further argues that concerning the general article "Systems for identifying new drugs are often faulty", the conclusion of the article is that "cancer drug screening is turning almost exclusively toward defining molecular targets". Applicant asserts that this issue is not relevant because the instant invention is a therapeutic immunoconjugate which has a defined molecular target.

Applicant asserts that concerning another recited general article, Sci Am 1994, which teaches that tumors resists penetration by drugs, the immunoconjugate does not necessarily require that a cell be penetrated by a drug, e.g. a radioactive material.

Concerning Hartwell et al, which teaches that chemotherapeutic drugs must be selectively kill tumor cells, and said drugs are toxic to dividing cells, Applicant asserts that this is not an issue, because the claimed invention is targeted, and because the prostate-specific nature of the claimed immunoconjugate.

Concerning unpredictability of immunotherapy, i.e. cancer vaccines, since no claims are directed to cancer vaccines in the instant application, the issues are not related to the claims currently being reviewed.

Applicant s arguments set forth in paper No.14 have been considered but are not deemed to be persuasive for the following reasons:

Although there were many examples of immunoconjugates comprising antibodies and toxins being used to selectively kill cells, these examples are not applicable to the claimed invention, because different antibodies behave in vivo differently, and one cannot predict that the PROST 03 immunoconjugate used in the claimed method could be used successful in vivo for killing prostate cancer cells or for treating prostate cancer. This issue is clearly shown by White et al, who teach that for a successful immunotherapy, besides the specificity of the antigen, other following properties of the antigen should also be considered: The antigen should be present on all or near all of the malignant cells to allow effective targeting and to prevent a subpopulation of antigen-negative cells from proliferating. Further, antibodies have been developed against a broad spectrum of antigens, and whether the antigens shed, modulate or internalize influence the effectiveness of the administered antibody (p.126, second paragraph). Moreover, antigen internalization or downregulation can cause repeat dosing to be unsuccessful due to the disappearance of the antibody target (p.126, paragraph before last). Thus, although those skilled in the art at the time the invention was made were aware of these issues, these issues are inherent properties of the antigens, such as antigen shedding, modulating or internalization, and consequently the

inherent effectiveness of the immunoconjugate. Applicant however has not shown the properties of the antigens targeted by the antibodies used in the claimed method, such that one could predict the effectiveness of the immunoconjugate of the claimed method in targeting and preventing a subpopulation of antigen-negative cells from proliferating. Applicant has not addressed how to enhance the effectiveness of the immunoconjugate used in the claimed method, if the problem concerning the effectiveness of targeting exists. Thus since the properties or behavior of the antigens and the cancer cells to which the immunoconjugate of the claimed method are not known, it is unpredictable that the immunoconjugate used in the claimed method would effectively target cancer cells in adequate amount for a successful therapy in vivo.

Further, although the claimed method uses the same principle as that of WO 93/17715, due to this same problem of unpredicted targeting effectiveness, one cannot predict the effectiveness of the claimed method, because the claimed invention uses different target than that of WO 93/17715. Moreover, Applicant has not addressed the problems raised by WO 93/17715, which is applicable to the claimed method because prostate cancer is solid tumor, i.e. (1) solid tumors are generally impermeable to antibody-sized molecules ; (2) antibodies that enter the tumor mass do not distribute evenly because of the dense packing of tumor cells; and (3) antigen-deficient mutants can escape being killed by the immunotoxin and regrow (WO 93/17715, p. 4, lines 10-37).

Concerning the teaching of Gura et al that that "cancer drug screening is turning almost exclusively toward defining molecular targets", this teaching clearly applies to the

exact problem with claimed invention. That is there is no defining of the molecular targets by the instant application, e.g., the in vivo properties or behavior of the target cancer cells, and the in vivo properties or behavior of the target antigen, as discussed above and in previous Office action.

Concerning Applicant's assertion that the immunoconjugate does not necessarily require that a cell be penetrated by a drug, e.g. a radioactive material, it is noted that the claims are not limited to immunoconjugate of radioactive material.

Concerning the reference by Hartwell et al, who teach that an effective chemotherapeutic must selectively kill tumor cells, it is unpredictable that that the immunoconjugate of the claimed method actually could target cancer cells in an effective amount to kill cancer cells, for reasons set forth above, and in previous Office action.

Concerning cancer vaccines, although the claims are not specifically recite the language "vaccine", the issue and the unpredictability associated with immunotherapy of a vaccine would apply as well to the claimed method. That is tumor immunity and immune tolerance by a treated patient could a prevalent problem, such that the effectiveness of an immunotherapy could be cancelled. For example, the problem with antigen expression by tumor cells, as taught by Boon et al, of record, to which an immunoconjugate is supposed to bind.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

December 08, 2003